Cerebral autoregulation

- Comparative analysis of two newly established Cre rat lines, NeuN-Cre and Thy1-Cre, for neurological research
- Targeting microglia polarization with Chinese herb-derived natural compounds for neuroprotection in ischemic stroke
- Biological Barrier Models-on-Chips: A Novel Tool for Disease Research and Drug Discovery
- The prevention effect of prebiotics and probiotics on bisphenol A caused neurotoxicity and mood disorders from the perspective of regulating gut microbiota
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- High-Calorie Diet Consumption Induces Lac-Phe Changes in the Brain in a Time-of-Day Manner Independent of Exercise
- Biomolecular Basis of Life

Understanding cerebral autoregulation is crucial for managing patients with neurological conditions and designing interventions that support optimal brain perfusion.

Cerebral autoregulation is the ability of the brain to maintain a constant blood flow despite changes in blood pressure.

Key features

Vascular Tone Adjustment: Cerebral autoregulation involves the dilation or constriction of the blood vessels in the brain in response to changes in blood pressure. When blood pressure increases, the cerebral vessels constrict to prevent excessive blood flow, and when blood pressure decreases, they dilate to maintain adequate blood flow to the brain.

Goals

Maintaining Cerebral Perfusion: The primary goal of cerebral autoregulation is to maintain a stable cerebral perfusion, allowing the brain to receive a consistent supply of oxygen and nutrients. This is crucial for the normal functioning of brain cells.

Range of Autoregulation: The autoregulatory range varies among individuals but is typically around a mean arterial pressure (MAP) of 60-150 mmHg. Within this range, the cerebral blood flow remains relatively constant.

Etiology of Disturbation

Dysfunction in cerebral autoregulation can occur in acute brain injury, such as traumatic brain injury or stroke, and can lead to poor outcomes.

Impairment in Diseases: Conditions such as traumatic brain injury, ischemic stroke, subarachnoid

hemorrhage, and certain neurological disorders can impair cerebral autoregulation. In such cases, the brain may be more vulnerable to fluctuations in blood pressure, leading to potential complications.

Assessment

Techniques such as transcranial Doppler ultrasound, near-infrared spectroscopy, and imaging studies are often employed to assess cerebral autoregulation in clinical settings. Monitoring cerebral autoregulation is important, especially in critical care situations, to prevent further damage to brain tissue due to inadequate blood flow or excessive pressure.

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see Cerebrovascular pressure reactivity index

Most Inhalational agents reduce cerebral metabolism (except nitrous oxide) by suppressing neuronal activity. These agents disturb cerebral autoregulation and cause cerebral vasodilatation, which increases cerebral blood volume (CBV) and can increase ICP.

Neuroinflammation has been suggested as a potential mechanism underlying cerebral autoregulation dysfunction in these conditions. Particularly inflammation affecting the cerebral vasculature is an important cascade that occurs following acute injury. Smith et al. hypothesize that disturbances to the cerebral vasculature can affect the regulation of CBF, and hence the vascular inflammatory pathways could be a putative mechanism that causes CA dysfunction [1)]

Some candidate neuroinflammatory markers of cerebral autoregulation dysfunction in human acute brain injury include:

Tumor necrosis factor-alpha (TNF-α): TNF-α is a pro-inflammatory cytokine that has been shown to disrupt cerebral autoregulation in animal studies. Elevated levels of TNF-α have also been observed in patients with traumatic brain injury and stroke.

Interleukin-6 (IL-6): IL-6 is another pro-inflammatory cytokine that has been implicated in cerebral autoregulation dysfunction. Elevated levels of IL-6 have been observed in patients with traumatic brain injury and stroke.

Matrix metalloproteinases (MMPs): MMPs are enzymes that play a role in the breakdown of the blood-brain barrier and extracellular matrix. Increased levels of MMPs have been observed in patients with traumatic brain injury and stroke and have been linked to cerebral autoregulation dysfunction.

S100B: S100B is a calcium-binding protein that is released by astrocytes in response to brain injury. Elevated levels of S100B have been observed in patients with traumatic brain injury and stroke and have been associated with cerebral autoregulation dysfunction.

Reactive oxygen species (ROS): ROS are highly reactive molecules that can cause oxidative damage to cells. Increased levels of ROS have been observed in patients with traumatic brain injury and stroke and have been linked to cerebral autoregulation dysfunction.

Overall, these candidate neuroinflammatory markers may provide insights into the underlying mechanisms of cerebral autoregulation dysfunction in acute brain injury and could potentially serve as targets for therapeutic interventions. However, further research is needed to fully understand the complex relationship between neuroinflammation and cerebral autoregulation dysfunction in these conditions

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Cerebrovascular autoregulation (CA) is an important hemodynamic mechanism that protects the brain against inappropriate fluctuations in cerebral blood flow in the face of changing cerebral perfusion pressure.

While most systems of the body show some degree of autoregulation, the brain is very sensitive to over- and underperfusion.

Brain perfusion is essential for life since the brain has a high metabolic demand. By means of cerebrovascular autoregulation the body is able to deliver sufficient blood containing oxygen and nutrients to the brain tissue for this metabolic need, and remove CO2 and other waste products.

However, due to the important influences of arterial carbon dioxide levels, cerebral metabolic rate, neural activation, activity of the sympathetic nervous system, posture, as well as other physiological variables, cerebral autoregulation is often interpreted as encompassing the wider field of cerebral blood flow regulation. This field includes areas such as CO2 reactivity, neurovascular coupling and other aspects of cerebral haemodynamics.

This regulation of cerebral blood flow is achieved primarily by small arteries, arterioles, which either dilate or contract under the influence of multiple complex physiological control systems.

Impairment of these systems may occur e.g. following stroke, trauma or anaesthesia, in premature babies and has been implicated in the development of subsequent brain injury.

Cerebral autoregulation disturbance after traumatic brain injury is associated with worse outcome.

Autonomic impairment after acute traumatic brain injury has been associated independently with both increased morbidity and mortality. Links between autonomic impairment and increased intracranial pressure or impaired cerebral autoregulation have been described as well. However, relationships between autonomic impairment, intracranial pressure, impaired cerebral autoregulation, and outcome remain poorly explored.

The non-invasive measurement of relevant physiological signals like cerebral blood flow, intracranial pressure, blood pressure, CO2 levels, cerebral oxygen consumption, etc. is challenging. Even more so, the subsequent assessment of the control systems. Much remains unknown about the physiology of blood flow control and the best clinical interventions to optimize patient outcome.

Classification

Static Cerebral Autoregulation:

Time Scale: Static cerebral autoregulation primarily operates over a more extended time scale.

Response to Changes in Mean Arterial Pressure (MAP): It deals with the ability of the cerebral vessels to maintain a relatively constant cerebral blood flow (CBF) in response to changes in mean arterial pressure (MAP) over longer periods. Purpose: The goal of static autoregulation is to ensure a consistent blood flow to the brain over time, preventing either excessive perfusion or inadequate supply. Dynamic Cerebral Autoregulation:

Time Scale: Dynamic cerebral autoregulation operates over shorter time intervals. Response to Rapid Changes: It focuses on the brain's ability to respond to rapid fluctuations in blood pressure, such as those occurring with each cardiac cycle. Purpose: Dynamic autoregulation helps to stabilize CBF during quick changes in blood pressure, ensuring that the brain receives a relatively steady supply of blood and oxygen. In summary, while static cerebral autoregulation deals with more prolonged changes in blood pressure to maintain stable blood flow over time, dynamic cerebral autoregulation addresses rapid, short-term fluctuations in blood pressure. Both components work together to safeguard the brain against hypoperfusion or hyperperfusion, contributing to the overall stability of cerebral blood flow in various physiological conditions and pathological states.

Complications

Increased cerebral blood volume: may result from loss of cerebral vascular autoregulation. This hyperemia may sometimes occur with extreme rapidity, in which case it has sometimes been referred to as diffuse or “malignant cerebral edema,” which carries close to 100% mortality and may be more common in children. Management consists of aggressive measures to maintain ICP < 22 mm Hg and CPP > 60-70 mm Hg. (whether 60 or 70 is the optimal minimum for CPP is unclear).

Monitoring

Pressure reactivity is a fundamental component of cerebral autoregulation that can be estimated using the pressure reactivity index, a correlation between slow arterial blood pressure, and intracranial pressure fluctuations.

Continuous monitoring of cerebral autoregulation might provide novel treatment targets and identify therapeutic windows after acute brain injury.

Slow oscillations of cerebral hemodynamics (0.05-0.003 Hz) are visible in Multimodal neuromonitoring and may be analyzed to provide novel, surrogate measures of autoregulation. Near-infrared spectroscopy (NIRS) is an optical neuromonitoring technique, which shows promise for widespread clinical applicability because it is noninvasive and easily delivered across a wide range of clinical scenarios.

Twenty-seven sedated, ventilated, brain-injured patients were included in this observational study. Intracranial pressure, transcranial Doppler-derived flow velocity in the middle cerebral artery, and ipsilateral cerebral NIRS variables were continuously monitored. Signals were compared using wavelet measures of phase and coherence to examine the spectral features involved in reactivity index calculations. Established indices of autoregulatory reserve such as the pressure reactivity index (PRx) and mean velocity index (Mx) and the NIRS indices such as total hemoglobin reactivity index (THx) and tissue oxygen reactivity index (TOx) were compared using correlation and Bland-Altman analysis.

NIRS indices correlated significantly between PRx and THx ($r_s = 0.63$, $P < 0.001$), PRx and TOx ($r =$

0.40, P = 0.04), and Mx and TOx (r = 0.61, P = 0.004) but not between Mx and THx (rs = 0.26, P = 0.28) and demonstrated wide limits between these variables: PRx and THx (bias, -0.06; 95% limits, -0.44 to 0.32) and Mx and TOx (bias, +0.15; 95% limits, -0.34 to 0.64). Analysis of slow-wave activity throughout the intracranial pressure, transcranial Doppler, and NIRS recordings revealed statistically significant interrelationships, which varied dynamically and were nonsignificant at frequencies <0.008 Hz.

Although slow-wave activity in intracranial pressure, transcranial Doppler, and NIRS is significantly similar, it varies dynamically in both time and frequency, and this manifests as incomplete agreement between reactivity indices. Analysis informed by a priori knowledge of physiology underpinning NIRS variables combined with sophisticated analysis techniques has the potential to deliver noninvasive surrogate measures of autoregulation, guiding therapy [2)].

Early deterioration of CA significantly correlates with unfavorable clinical outcome and severity of angiographic vasospasm. Dynamic CA measurements might represent an important tool in stratifying therapy guidelines in patients after SAH [3)].

Unfavorable outcomes for Traumatic Brain Injury (TBI) patients are more significantly associated with the duration of the single longest CA impairment episode at a high pressure reactivity index [PRx(t)] value, rather than with averaged PRx(t) values or the average time of all CA impairment episodes [4)].

Cerebral perfusion pressure and cerebral autoregulation

Secondary brain injury (i.e., following the initial trauma) is attributable in part to cerebral ischemia. The critical parameter for brain function and survival is not actually ICP, rather is adequate cerebral blood flow (CBF) to meet CMRO2 demands.

CBF is difficult to quantitate, and can only be measured continuously at the bedside with specialized equipment and difficulty. However, CBF depends on cerebral perfusion pressure (CPP), which is related to ICP (which is more easily measured)

The actual pressure of interest is the mean carotid pressure (MCP) which may be approximated as the MAP with the transducer zeroed ≈ at the level of the foramen of Monro.

As ICP becomes elevated, CPP is reduced at any given MAP. Normal adult CPP is > 50 mm Hg. Cerebral autoregulation is a mechanism whereby over a wide range, large changes in systemic BP produce only small changes in CBF. Due to autoregulation, CPP would have to drop below 40 in a normal brain before CBF would be impaired.

In the head-injured patient, older recommendations were to maintain CPP ≥ 70 mm Hg (due to increased cerebral vascular resistance) & ICP < 20 mm Hg.3 However, recent evidence suggests that elevated ICP (≥ 22 mm Hg) may be more detrimental than changes in CPP (as long as CPP is > 60-70 mm Hg) (higher levels of CPP were not protective against significant ICP elevations).

Neonatal cerebrovascular autoregulation

see Neonatal cerebrovascular autoregulation.

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